```
=> File .Biotech

=> s (memapsin 2 or beta secretase or beta amyloid precursor protein or APP)
L1      630677 (MEMAPSIN 2 OR BETA SECRETASE OR BETA AMYLOID PRECURSOR PROTEIN
               OR APP)

=> s (l1 or memapsin 2) and (OM 99 or OM-99 or dipeptide isostere or dipeptide or
isostere) and Alzheimer?
L2          135 (L1 OR MEMAPSIN 2) AND (OM 99 OR OM-99 OR DIPEPTIDE ISOSTERE OR
               DIPEPTIDE OR ISOSTERE) AND ALZHEIMER?

=> s l2 and (computer program# or software program#)
L3           22 L2 AND (COMPUTER PROGRAM# OR SOFTWARE PROGRAM#)

=> s l3 and (recombinant?)
L4           22 L3 AND (RECOMBINANT?)

=> s l4 and (treat? or therapeut? or diagnos? or prevent?)
   5 FILES SEARCHED...
L5           22 L4 AND (TREAT? OR THERAPEUT? OR DIAGNOS? OR PREVENT?)

=> s l5 and (inhibit?)
L6           22 L5 AND (INHIBIT?)

=> s Tang J?/au; s Hong L/au; s Ghosh A/au; s Koelsch G/au
L7         8203 TANG J?/AU


L8          417 HONG L/AU


L9         1933 GHOSH A/AU


L10         100 KOELSCH G/AU

=> s l6 and (l7 or l8 or l9 or l10)
L11           7 L6 AND (L7 OR L8 OR L9 OR L10)

=> d l11 1-7 bib ab

L11  ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2003 ACS on STN
AN   2001:12489  CAPLUS
DN   134:80832
TI   Inhibitors of memapsin 2 and use thereof
IN   Tang, Jordan J. N.; Hong, Ling; Ghosh, Arun K.
PA   Oklahoma Medical Research Foundation, USA; The Board of Trustees of the
     University of Illinois
SO   PCT Int. Appl., 86 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 3
     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
     ---------------    ----  --------       ---------------  --------
PI   WO 2001000665      A2    20010104       WO 2000-US17742  20000627
     WO 2001000665      A3    20010927
     WO 2001000665      C2    20020725
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
             SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
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DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|---|
| EP 1194449 | A2 | 20020410 | EP 2000-943236 | 20000627 | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | | |
| JP 2003506322 | T2 | 20030218 | JP 2001-507071 | 20000627 | |
| US 6545127 | B1 | 20030408 | US 2000-604608 | 20000627 | |
| US 2002049303 | A1 | 20020425 | US 2001-796264 | 20010228 | |
| US 2002164760 | A1 | 20021107 | US 2001-795903 | 20010228 | |
| US 2002115600 | A1 | 20020822 | US 2001-845226 | 20010430 | |
| PRAI US 1999-141363P | P | 19990628 | | | |
| US 1999-168060P | P | 19991130 | | | |
| US 2000-177836P | P | 20000125 | | | |
| US 2000-178368P | P | 20000127 | | | |
| US 2000-210292P | P | 20000608 | | | |
| US 2000-603713 | A3 | 20000627 | | | |
| US 2000-604608 | A3 | 20000627 | | | |
| WO 2000-US17742 | W | 20000627 | | | |

AB Methods for the prodn. of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been detd. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogs including isosteres at the sites of the crit. amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (Figure 1). The **inhibition** const. of OM99-2 is 1.6 x 10-9 M against **recombinant** pro-**memapsin 2**. Crystallog. of **memapsin 2** bound to this **inhibitor** was used to det. the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using com. available **software programs** and techniques familiar to those in org. chem. and enzymol., to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L11 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:12487 CAPLUS
DN 134:68049
TI Catalytically active **recombinant memapsin 2**, 3D crystal structure based **inhibitor** design, synthesis, and screening, for **Alzheimer**'s disease **treatment**
IN **Tang, Jordan J. N.**; Lin, Xinli; Koelsch, Gerald
PA Oklahoma Medical Research Foundation, USA
SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001000663 | A2 | 20010104 | WO 2000-US17661 | 20000627 |
| WO 2001000663 | A3 | 20011004 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, | | | | |

IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|---|
| EP 1196609 | A2 | 20020417 | EP 2000-943208 | 20000627 | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | | |
| JP 2003503072 | T2 | 20030128 | JP 2001-507069 | 20000627 | |
| US 6545127 | B1 | 20030408 | US 2000-604608 | 20000627 | |
| US 2002049303 | A1 | 20020425 | US 2001-796264 | 20010228 | |
| US 2002164760 | A1 | 20021107 | US 2001-795903 | 20010228 | |
| US 2002115600 | A1 | 20020822 | US 2001-845226 | 20010430 | |
| PRAI US 1999-141363P | P | 19990628 | | | |
| US 1999-168060P | P | 19991130 | | | |
| US 2000-177836P | P | 20000125 | | | |
| US 2000-178368P | P | 20000127 | | | |
| US 2000-210292P | P | 20000608 | | | |
| US 2000-603713 | A3 | 20000627 | | | |
| US 2000-604608 | A3 | 20000627 | | | |
| WO 2000-US17661 | W | 20000627 | | | |

AB A method for producing catalytically active **recombinant memapsin 2** comprising expression in a bacteria and refolding the **recombinant memapsin 2** under conditions which dissoc. and then slowly refold the enzyme into a catalytically active form is disclosed. A method of isolating **inhibitors** of cleavage by **memapsin 2** comprising adding to one or more potential **inhibitors** of catalytically active **recombinant memapsin 2** , and a substrate for **memapsin 2**, and screening for decreased cleavage of the substrate by the **inhibitors**, wherein the **inhibitors** are in a library of small synthetic mols., like proteins and peptides. Alternatively, the **inhibitors** are oligonucleotides **preventing** or decreasing expression of catalytically active **memapsin 2**. A method for designing or obtaining **inhibitors** of catalytically active **memapsin 2** comprising modeling an **inhibitor** based on the crystn. coordinates of **memapsin 2** or parameters. A database comprising binding properties and chem. structures of compds. designed or screened by modeling an **inhibitor** based on the crystn. coordinates of **memapsin 2** or parameters is claimed. A method of **treating** or **preventing** **Alzheimer**'s disease comprising administering to a patient in need thereof an **inhibitor** of **memapsin 2** which binds to the active site of the **memapsin 2** defined by the presence of two catalytic aspartic residues and substrate binding cleft, is also claimed. The cDNAs of two new human membrane-assocd. aspartic proteases, memapsin 1 and **memapsin 2**, have been cloned and sequenced. The substrate and subsite specificity of the catalytically active enzyme have been detd. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogs including isosteres at the sites of the crit. amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (Fig. 1). The **inhibition** const. of OM99-2 is 1.6 x 109 M

against **recombinant** pro-**memapsin 2**.
Crystallog. of **memapsin 2** bound to this
**inhibitor** was used to det. the three dimensional structure of the
protein, as well as the importance of the various residues in binding.
This information can be used to design new **inhibitors**, using
com. available **software programs** and techniques
familiar to those in org. chem. and enzymol., to design new
**inhibitors** to **memapsin 2**, useful in
**diagnostics** and for the **treatment** and/or
**prevention** of **Alzheimer**'s disease.

L11 ANSWER 3 OF 7 USPATFULL on STN
AN 2003:134541 USPATFULL
TI **Inhibitors** of **memapsin 2** and use thereof
IN **Tang, Jordan J. N.**, Edmond, OK, UNITED STATES
Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Ghosh, Arun K., River Forest, IL, UNITED STATES
PA Oklahoma Medical Research Foundation, Oklahoma City, OK (U.S. corporation)
PI US 2003092629 A1 20030515
AI US 2001-32818 A1 20011228 (10)
PRAI US 2001-275756P 20010314 (60)
US 2000-258705P 20001228 (60)
DT Utility
FS APPLICATION
LREP HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 2203
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed-, The substrate and subsite specificity of the catalytically active enzyme have been determined by a method which determines the initial hydrolysis rate of the substrates by using MALDI-TOF/MS. Alternatively, the subsite specificity of memapsin can be determined by probing a library of **inhibitors** with **memapsin 2** and subsequently detecting the bound **memapsin 2** with an antibody raised to **memapsin 2** and an alkaline phosphatase conjugated secondary antibody. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the more than seventy substrate analogues were synthesized, among which MMI-005, MMI-012, MMI-017, MMI-018, MMI-025, MMI-026, MMI-037, MMI-039, MMI-040, MMI-066, MMI-070, and MMI-071 have **inhibition** constants in the range of 1.4-61.4.times.10.sup.-9 M against **recombinant** pro-**memapsin 2**. These **inhibitors** are useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L11 ANSWER 4 OF 7 USPATFULL on STN
AN 2003:96167 USPATFULL
TI Catalytically active **recombinant** memapsin and methods of use thereof
IN **Tang, Jordan J. N.**, Edmond, OK, United States
Lin, Xinli, Edmond, OK, United States

Koelsch, Gerald, Oklahoma City, OK, United States
Hong, Lin, Oklahoma City, OK, United States
PA Oklahoma Medical Research Foundation, Oklahoma City, OK, United States (U.S. corporation)
PI US 6545127 B1 20030408
AI US 2000-604608 20000627 (9)
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Borin, Michael; Assistant Examiner: Zhou, Shuba
LREP Hamilton, Brook, Smith & Reynolds, P.C.
CLMN Number of Claims: 18
ECL Exemplary Claim: 7
DRWN 21 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 2563
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6.times.10.sup.-9M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L11 ANSWER 5 OF 7 USPATFULL on STN
AN 2002:294717 USPATFULL
TI Catalytically active **recombinant** memapsin and methods of use thereof
IN Lin, Xinli, Edmond, OK, UNITED STATES
Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
**Tang, Jordan J.N.**, Edmond, OK, UNITED STATES
PA Oklahoma Medical Research Foundation
PI US 2002164760 A1 20021107
AI US 2001-795903 A1 20010228 (9)
RLI Division of Ser. No. US 2000-604608, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)

DT Utility
FS APPLICATION
LREP PATREA L. PABST, HOLLAND & KNIGHT LLP, SUITE 2000, ONE ATLANTIC CENTER, 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA, 30309-3400
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2440
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6.times.10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L11 ANSWER 6 OF 7 USPATFULL on STN
AN 2002:214213 USPATFULL
TI **Inhibitors** of **memapsin 2** and use thereof
IN Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
**Tang, Jordan J.N.**, Edmond, OK, UNITED STATES
Hong, Lin, Oklahoma City, OK, UNITED STATES
Ghosh, Arun K., River Forest, IL, UNITED STATES
PA Oklahoma Medical Research Foundation (U.S. corporation)
PI US 2002115600 A1 20020822
AI US 2001-845226 A1 20010430 (9)
RLI Division of Ser. No. US 2000-603713, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)
DT Utility
FS APPLICATION
LREP Patrea L. Pabst, Arnall Golden & Gregory, LLP, 2800 One Atlantic Center, 1201 West Peachtree Street, Atlanta, GA, 30309-3450
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2377
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed.

The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6.times.10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the tliree dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L11 ANSWER 7 OF 7 USPATFULL on STN
AN 2002:92777 USPATFULL
TI Catalytically active **recombinant** memapsin and methods of use thereof
IN **Tang, Jordan J. N.**, Edmond, OK, UNITED STATES
Lin, Xinli, Edmond, OK, UNITED STATES
Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Hong, Lin, Oklahoma City, OK, UNITED STATES
PI US 2002049303 A1 20020425
AI US 2001-796264 A1 20010228 (9)
RLI Division of Ser. No. US 2000-604608, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
DT Utility
FS APPLICATION
LREP PATREA L. PABST, HOLLAND & KNIGHT LLP, SUITE 2000, ONE ATLANTIC CENTER, 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA, 30309-3400
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2441
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogs including isosteres at the sites of the critical amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide

Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6.times.10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

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=> d his

     (FILE 'HOME' ENTERED AT 16:27:26 ON 05 AUG 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, BIOTECHDS, EMBASE, USPATFULL, WPIDS'
     ENTERED AT 16:29:30 ON 05 AUG 2003
L1       630677 S (MEMAPSIN 2 OR BETA SECRETASE OR BETA AMYLOID PRECURSOR PROTE
L2          135 S (L1 OR MEMAPSIN 2) AND (OM 99 OR OM-99 OR DIPEPTIDE ISOSTERE
L3           22 S L2 AND (COMPUTER PROGRAM# OR SOFTWARE PROGRAM#)
L4           22 S L3 AND (RECOMBINANT?)
L5           22 S L4 AND (TREAT? OR THERAPEUT? OR DIAGNOS? OR PREVENT?)
L6           22 S L5 AND (INHIBIT?)
L7         8203 S TANG J?/AU
L8          417 S HONG L/AU
L9         1933 S GHOSH A/AU
L10         100 S KOELSCH G/AU
L11           7 S L6 AND (L7 OR L8 OR L9 OR L10)

=> d l6 1-22 bib ab

L6   ANSWER 1 OF 22  CAPLUS  COPYRIGHT 2003 ACS on STN
AN   2001:12489  CAPLUS
DN   134:80832
TI   Inhibitors of memapsin 2 and use thereof
IN   Tang, Jordan J. N.; Hong, Ling; Ghosh, Arun K.
PA   Oklahoma Medical Research Foundation, USA; The Board of Trustees of the
     University of Illinois
SO   PCT Int. Appl., 86 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 3
     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
     ---------------    ----  --------       ---------------  --------
PI   WO 2001000665      A2    20010104       WO 2000-US17742  20000627
     WO 2001000665      A3    20010927
     WO 2001000665      C2    20020725
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
             SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1194449          A2    20020410       EP 2000-943236   20000627
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
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| | | | | | |
|---|---|---|---|---|---|
| | JP 2003506322 | T2 | 20030218 | JP 2001-507071 | 20000627 |
| | US 6545127 | B1 | 20030408 | US 2000-604608 | 20000627 |
| | US 2002049303 | A1 | 20020425 | US 2001-796264 | 20010228 |
| | US 2002164760 | A1 | 20021107 | US 2001-795903 | 20010228 |
| | US 2002115600 | A1 | 20020822 | US 2001-845226 | 20010430 |
| PRAI | US 1999-141363P | P | 19990628 | | |
| | US 1999-168060P | P | 19991130 | | |
| | US 2000-177836P | P | 20000125 | | |
| | US 2000-178368P | P | 20000127 | | |
| | US 2000-210292P | P | 20000608 | | |
| | US 2000-603713 | A3 | 20000627 | | |
| | US 2000-604608 | A3 | 20000627 | | |
| | WO 2000-US17742 | W | 20000627 | | |

AB Methods for the prodn. of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been detd. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogs including isosteres at the sites of the crit. amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (Figure 1). The **inhibition** const. of OM99-2 is 1.6 x 10-9 M against **recombinant** pro-**memapsin 2**. Crystallog. of **memapsin 2** bound to this **inhibitor** was used to det. the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using com. available **software programs** and techniques familiar to those in org. chem. and enzymol., to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L6 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:12487 CAPLUS
DN 134:68049
TI Catalytically active **recombinant memapsin 2**, 3D crystal structure based **inhibitor** design, synthesis, and screening, for **Alzheimer**'s disease **treatment**
IN Tang, Jordan J. N.; Lin, Xinli; Koelsch, Gerald
PA Oklahoma Medical Research Foundation, USA
SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2001000663 | A2 | 20010104 | WO 2000-US17661 | 20000627 |
| | WO 2001000663 | A3 | 20011004 | | |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| EP 1196609 | A2 | 20020417 | EP 2000-943208 | 20000627 | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | | |
| JP 2003503072 | T2 | 20030128 | JP 2001-507069 | 20000627 | |
| US 6545127 | B1 | 20030408 | US 2000-604608 | 20000627 | |
| US 2002049303 | A1 | 20020425 | US 2001-796264 | 20010228 | |
| US 2002164760 | A1 | 20021107 | US 2001-795903 | 20010228 | |
| US 2002115600 | A1 | 20020822 | US 2001-845226 | 20010430 | |
| PRAI US 1999-141363P | P | 19990628 | | | |
| US 1999-168060P | P | 19991130 | | | |
| US 2000-177836P | P | 20000125 | | | |
| US 2000-178368P | P | 20000127 | | | |
| US 2000-210292P | P | 20000608 | | | |
| US 2000-603713 | A3 | 20000627 | | | |
| US 2000-604608 | A3 | 20000627 | | | |
| WO 2000-US17661 | W | 20000627 | | | |

AB A method for producing catalytically active **recombinant** **memapsin 2** comprising expression in a bacteria and refolding the **recombinant** **memapsin 2** under conditions which dissoc. and then slowly refold the enzyme into a catalytically active form is disclosed. A method of isolating **inhibitors** of cleavage by **memapsin 2** comprising adding to one or more potential **inhibitors** of catalytically active **recombinant** **memapsin 2** , and a substrate for **memapsin 2**, and screening for decreased cleavage of the substrate by the **inhibitors**, wherein the **inhibitors** are in a library of small synthetic mols., like proteins and peptides. Alternatively, the **inhibitors** are oligonucleotides **preventing** or decreasing expression of catalytically active **memapsin 2**. A method for designing or obtaining **inhibitors** of catalytically active **memapsin 2** comprising modeling an **inhibitor** based on the crystn. coordinates of **memapsin 2** or parameters. A database comprising binding properties and chem. structures of compds. designed or screened by modeling an **inhibitor** based on the crystn. coordinates of **memapsin 2** or parameters is claimed. A method of **treating** or **preventing** **Alzheimer**'s disease comprising administering to a patient in need thereof an **inhibitor** of **memapsin 2** which binds to the active site of the **memapsin 2** defined by the presence of two catalytic aspartic residues and substrate binding cleft, is also claimed. The cDNAs of two new human membrane-assocd. aspartic proteases, memapsin 1 and **memapsin 2**, have been cloned and sequenced. The substrate and subsite specificity of the catalytically active enzyme have been detd. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogs including isosteres at the sites of the crit. amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (Fig. 1). The **inhibition** const. of OM99-2 is 1.6 x 109 M against **recombinant** pro-**memapsin 2**. Crystallog. of **memapsin 2** bound to this **inhibitor** was used to det. the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used to design new **inhibitors**, using

com. available **software programs** and techniques familiar to those in org. chem. and enzymol., to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L6 ANSWER 3 OF 22 USPATFULL on STN
AN 2003:200784 USPATFULL
TI Immunogenic HBc chimer particles having enhanced stability
IN Birkett, Ashley J., Escondido, CA, UNITED STATES
PI US 2003138769 A1 20030724
AI US 2001-930915 A1 20010815 (9)
RLI Continuation-in-part of Ser. No. US 2000-226867, filed on 22 Aug 2000, PENDING Continuation-in-part of Ser. No. US 2000-225843, filed on 16 Aug 2000, PENDING
DT Utility
FS APPLICATION
LREP WELSH & KATZ, LTD, 120 S RIVERSIDE PLAZA, 22ND FLOOR, CHICAGO, IL, 60606
CLMN Number of Claims: 115
ECL Exemplary Claim: 1
DRWN 10 Drawing Page(s)
LN.CNT 6993
AB A chimeric, carboxy-terminal truncated hepatitis B virus nucleocapsid protein (HBc) is disclosed that is engineered for both enhanced stability of self-assembled particles and the display of an immunogenic epitope. The display of the immunogenic epitope is displayed in the immunogenic loop of HBc, whereas the enhanced stability of self-assembled particles is obtained by the presence of at least one heterologous cysteine residue near the carboxy-terminus of the chimer molecule. Methods of making and using the chimers are also disclosed.

L6 ANSWER 4 OF 22 USPATFULL on STN
AN 2003:187895 USPATFULL
TI 12 human secreted proteins
IN Ni, Jian, Germantown, MD, UNITED STATES
Young, Paul E., Gaithersburg, MD, UNITED STATES
Kenny, Joseph J., Damascus, MD, UNITED STATES
Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
Moore, Paul A., Germantown, MD, UNITED STATES
Wei, Ying-Fei, Berkeley, CA, UNITED STATES
Greene, John M., Gaithersburg, MD, UNITED STATES
Ruben, Steven M., Olney, MD, UNITED STATES
PI US 2003129685 A1 20030710
AI US 2001-836353 A1 20010418 (9)
RLI Continuation-in-part of Ser. No. WO 1999-US25031, filed on 27 Oct 1999, UNKNOWN
PRAI US 1998-105971P 19981028 (60)
US 2000-198407P 20000419 (60)
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 59 Drawing Page(s)
LN.CNT 31945
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and **recombinant** methods for producing human secreted proteins. The invention further relates to **diagnostic** and **therapeutic** methods useful for **diagnosing** and **treating** diseases, disorders, and/or conditions related to these novel human secreted proteins.

L6 ANSWER 5 OF 22 USPATFULL on STN
AN 2003:165862 USPATFULL
TI Directed evolution of novel binding proteins
IN Ladner, Robert Charles, Ijamsville, MD, UNITED STATES
Guterman, Sonia Kosow, Belmont, MA, UNITED STATES
Roberts, Bruce Lindsay, Milford, MA, UNITED STATES
Markland, William, Milford, MA, UNITED STATES
Ley, Arthur Charles, Newton, MA, UNITED STATES
Kent, Rachel Baribault, Boxborough, MA, UNITED STATES
PI US 2003113717 A1 20030619
AI US 2001-893878 A1 20010629 (9)
RLI Continuation of Ser. No. US 1997-993776, filed on 18 Dec 1997, PENDING
Continuation of Ser. No. US 1995-415922, filed on 3 Apr 1995, PATENTED
Continuation of Ser. No. US 1993-9319, filed on 26 Jan 1993, PATENTED
Division of Ser. No. US 1991-664989, filed on 1 Mar 1991, PATENTED
Continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990, ABANDONED Continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988, ABANDONED
PRAI WO 1989-US3731 19890901
DT Utility
FS APPLICATION
LREP BROWDY AND NEIMARK, P.L.L.C., 624 Ninth Street, N.W., Washington, DC, 20001
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN 16 Drawing Page(s)
LN.CNT 15933
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural-signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin **inhibitor**, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

L6 ANSWER 6 OF 22 USPATFULL on STN
AN 2003:134541 USPATFULL
TI **Inhibitors** of **memapsin 2** and use thereof
IN Tang, Jordan J. N., Edmond, OK, UNITED STATES
Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Ghosh, Arun K., River Forest, IL, UNITED STATES
PA Oklahoma Medical Research Foundation, Oklahoma City, OK (U.S. corporation)
PI US 2003092629 A1 20030515
AI US 2001-32818 A1 20011228 (10)
PRAI US 2001-275756P 20010314 (60)
US 2000-258705P 20001228 (60)
DT Utility
FS APPLICATION
LREP HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)

LN.CNT 2203
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed-, The substrate and subsite specificity of the catalytically active enzyme have been determined by a method which determines the initial hydrolysis rate of the substrates by using MALDI-TOF/MS. Alternatively, the subsite specificity of memapsin can be determined by probing a library of **inhibitors** with **memapsin 2** and subsequently detecting the bound **memapsin 2** with an antibody raised to **memapsin 2** and an alkaline phosphatase conjugated secondary antibody. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the more than seventy substrate analogues were synthesized, among which MMI-005, MMI-012, MMI-017, MMI-018, MMI-025, MMI-026, MMI-037, MMI-039, MMI-040, MMI-066, MMI-070, and MMI-071 have **inhibition** constants in the range of 1.4-61.4.times.10.sup.-9 M against **recombinant** pro-**memapsin 2**. These **inhibitors** are useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L6 ANSWER 7 OF 22 USPATFULL on STN
AN 2003:96167 USPATFULL
TI Catalytically active **recombinant** memapsin and methods of use thereof
IN Tang, Jordan J. N., Edmond, OK, United States
Lin, Xinli, Edmond, OK, United States
Koelsch, Gerald, Oklahoma City, OK, United States
Hong, Lin, Oklahoma City, OK, United States
PA Oklahoma Medical Research Foundation, Oklahoma City, OK, United States (U.S. corporation)
PI US 6545127 B1 20030408
AI US 2000-604608 20000627 (9)
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Borin, Michael; Assistant Examiner: Zhou, Shuba
LREP Hamilton, Brook, Smith & Reynolds, P.C.
CLMN Number of Claims: 18
ECL Exemplary Claim: 7
DRWN 21 Drawing Figure(s); 12 Drawing Page(s)
LN.CNT 2563
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by

**memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6.times.10.sup.-9M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L6 ANSWER 8 OF 22 USPATFULL on STN
AN 2003:79303 USPATFULL
TI 12 human secreted proteins
IN Ni, Jian, Germantown, MD, UNITED STATES
Young, Paul E., Gaithersburg, MD, UNITED STATES
Kenny, Joseph J., Damascus, MD, UNITED STATES
Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
Moore, Paul A., Germantown, MD, UNITED STATES
Wei, Ying-Fei, Berkeley, CA, UNITED STATES
Greene, John M., Gaitherburg, MD, UNITED STATES
Ruben, Steven M., Olney, MD, UNITED STATES
Liu, Ding, Gaithersburg, MD, UNITED STATES
Crocker, Paul R., Dundee, UNITED KINGDOM
PI US 2003055231 A1 20030320
AI US 2001-984130 A1 20011029 (9)
RLI Continuation-in-part of Ser. No. US 2001-836353, filed on 18 Apr 2001, PENDING Continuation-in-part of Ser. No. WO 1999-US25031, filed on 27 Oct 1999, UNKNOWN
PRAI US 2000-243792P 20001030 (60)
US 2000-198407P 20000419 (60)
US 1998-105971P 19981028 (60)
DT Utility
FS APPLICATION
LREP HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 67 Drawing Page(s)
LN.CNT 31982
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to 12 novel human secreted proteins and isolated nucleic acids containing the coding regions of the genes encoding such proteins. Also provided are vectors, host cells, antibodies, and **recombinant** methods for producing human secreted proteins. The invention further relates to **diagnostic** and **therapeutic** methods useful for **diagnosing** and **treating** disorders related to these novel human secreted proteins.

L6 ANSWER 9 OF 22 USPATFULL on STN
AN 2003:4068 USPATFULL
TI Method of **preventing** cell death using segments of neural thread proteins
IN Averback, Paul A., Beaconsfield, CANADA
PI US 2003004107 A1 20030102
AI US 2002-146130 A1 20020516 (10)
PRAI US 2001-290971P 20010516 (60)

DT Utility
FS APPLICATION
LREP HUNTON & WILLIAMS, INTELLECTUAL PROPERTY DEPARTMENT, 1900 K STREET, N.W., SUITE 1200, WASHINGTON, DC, 20006-1109
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 1698
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed is a method of **preventing**, **inhibiting**, and/or ameliorating cell death and/or tissue necrosis in live tissue by contacting live tissue with at least a segment of NTP, or homologue, variant, derivative or mimetic thereof, where the segment of NTP, or homologue, variant, derivative or mimetic thereof is present in an amount effective to **prevent**, **inhibit**, and/or ameliorate cell death and/or tissue necrosis. The method is capable of **treating** conditions requiring **prevention**, **inhibition**, and/or amelioration of cell death and/or tissue necrosis.

L6 ANSWER 10 OF 22 USPATFULL on STN
AN 2003:3410 USPATFULL
TI Method of **preventing** cell death using antibodies to neural thread proteins
IN Averback, Paul A., Quebec, CANADA
PI US 2003003445 A1 20030102
AI US 2002-138516 A1 20020506 (10)
PRAI US 2001-288463P 20010504 (60)
DT Utility
FS APPLICATION
LREP HUNTON & WILLIAMS, INTELLECTUAL PROPERTY DEPARTMENT, 1900 K STREET, N.W., SUITE 1200, WASHINGTON, DC, 20006-1109
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 10 Drawing Page(s)
LN.CNT 1705
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed is a method of **preventing**, **inhibiting**, and/or ameliorating cell death and/or tissue necrosis in live tissue containing neural thread proteins (NTP) by contacting the live tissue with at least an antibody, antibody fragment or antibody derivative that recognizes or binds to NTP, where the antibody, antibody fragment or antibody derivative is present in an amount effective to **prevent**, **inhibit**, reduce, control and/or ameliorate cell death and/or tissue necrosis. The method is capable of **treating** conditions requiring **prevention**, **inhibition**, reduction, control and/or amelioration of cell death and/or tissue necrosis caused by the presence of NTP.

L6 ANSWER 11 OF 22 USPATFULL on STN
AN 2002:294717 USPATFULL
TI Catalytically active **recombinant** memapsin and methods of use thereof
IN Lin, Xinli, Edmond, OK, UNITED STATES
Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Tang, Jordan J.N., Edmond, OK, UNITED STATES
PA Oklahoma Medical Research Foundation
PI US 2002164760 A1 20021107
AI US 2001-795903 A1 20010228 (9)
RLI Division of Ser. No. US 2000-604608, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)

DT Utility
FS APPLICATION
LREP PATREA L. PABST, HOLLAND & KNIGHT LLP, SUITE 2000, ONE ATLANTIC CENTER, 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA, 30309-3400
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2440
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6.times.10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L6 ANSWER 12 OF 22 USPATFULL on STN
AN 2002:272761 USPATFULL
TI Directed evolution of novel binding proteins
IN Ladner, Robert Charles, Ijamsville, MD, UNITED STATES
Guterman, Sonia Kosow, Belmont, MA, UNITED STATES
Roberts, Bruce Lindsay, Milford, MA, UNITED STATES
Markland, William, Milford, MA, UNITED STATES
Ley, Arthur Charles, Newton, MA, UNITED STATES
Kent, Rachel Baribault, Boxborough, MA, UNITED STATES
PI US 2002150881 A1 20021017
AI US 2001-781988 A1 20010214 (9)
RLI Continuation of Ser. No. US 1998-192067, filed on 16 Nov 1998, ABANDONED Continuation of Ser. No. US 1995-415922, filed on 3 Apr 1995, PATENTED Continuation of Ser. No. US 1993-9319, filed on 26 Jan 1993, PATENTED Division of Ser. No. US 1991-664989, filed on 1 Mar 1991, PATENTED Continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990, ABANDONED Continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988, ABANDONED
PRAI WO 1989-US3731 19890901
DT Utility
FS APPLICATION
LREP BROWDY AND NEIMARK, P.L.L.C., 624 Ninth Street, N.W., Washington, DC, 20001
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN 16 Drawing Page(s)
LN.CNT 15696

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin **inhibitor**, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

L6 ANSWER 13 OF 22 USPATFULL on STN
AN 2002:265848 USPATFULL
TI Biopolymer sequence comparison
IN Toll, Lawrence R., Redwood City, CA, UNITED STATES
Lincoln, Patrick Denis, Woodside, CA, UNITED STATES
Karp, Peter, San Mateo, CA, UNITED STATES
Sonmez, Kemal, Menlo Park, CA, UNITED STATES
PI US 2002146724 A1 20021010
AI US 2001-6492 A1 20011203 (10)
PRAI US 2000-250743P 20001201 (60)
DT Utility
FS APPLICATION
LREP DAVID L. FEIGENBAUM, Fish & Richardson P.C., 225 Franklin Street, Boston, MA, 02110-2804
CLMN Number of Claims: 71
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 1796
AB Disclosed are methods, software, and systems for comparing biopolymer sequences. The model includes at least two different characterizations of states of matching between segments of sequences at defined positions. Examples of states of matching include: similarity and dissimilarity between objects, as well as similarity to a reference, e.g., a reference sequence or a sequence profile. A topology of particular match states can be used to identify classes of sequences, e.g., preprohormone sequences.

L6 ANSWER 14 OF 22 USPATFULL on STN
AN 2002:214213 USPATFULL
TI **Inhibitors** of **memapsin 2** and use thereof
IN Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Tang, Jordan J.N., Edmond, OK, UNITED STATES
Hong, Lin, Oklahoma City, OK, UNITED STATES
Ghosh, Arun K., River Forest, IL, UNITED STATES
PA Oklahoma Medical Research Foundation (U.S. corporation)
PI US 2002115600 A1 20020822
AI US 2001-845226 A1 20010430 (9)
RLI Division of Ser. No. US 2000-603713, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
US 2000-210292P 20000608 (60)
DT Utility
FS APPLICATION
LREP Patrea L. Pabst, Arnall Golden & Gregory, LLP, 2800 One Atlantic Center,

1201 West Peachtree Street, Atlanta, GA, 30309-3450
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2377
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogues including isosteres at the sites of the critical amino acid residues were developed and the substrate analogues, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6.times.10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the tliree dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L6 ANSWER 15 OF 22 USPATFULL on STN
AN 2002:191539 USPATFULL
TI Full-length human cDNAs encoding potentially secreted proteins
IN Milne Edwards, Jean-Baptiste Dumas, Paris, FRANCE
Bougueleret, Lydie, Petit Lancy, SWITZERLAND
Jobert, Severin, Paris, FRANCE
PI US 2002102604 A1 20020801
AI US 2000-731872 A1 20001207 (9)
PRAI US 1999-169629P 19991208 (60)
US 2000-187470P 20000306 (60)
DT Utility
FS APPLICATION
LREP John Lucas, Ph.D., J.D., Genset Corporation, 10665 Srrento Valley Road, San Diego, CA, 92121-1609
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 28061
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns GENSET polynucleotides and polypeptides. Such GENSET products may be used as reagents in forensic analyses, as chromosome markers, as tissue/cell/organelle-specific markers, in the production of expression vectors. In addition, they may be used in screening and **diagnosis** assays for abnormal GENSET expression and/or biological activity and for screening compounds that may be used in the **treatment** of GENSET-related disorders.

L6 ANSWER 16 OF 22 USPATFULL on STN
AN 2002:92777 USPATFULL
TI Catalytically active **recombinant** memapsin and methods of use

thereof
IN Tang, Jordan J. N., Edmond, OK, UNITED STATES
Lin, Xinli, Edmond, OK, UNITED STATES
Koelsch, Gerald, Oklahoma City, OK, UNITED STATES
Hong, Lin, Oklahoma City, OK, UNITED STATES
PI US 2002049303 A1 20020425
AI US 2001-796264 A1 20010228 (9)
RLI Division of Ser. No. US 2000-604608, filed on 27 Jun 2000, PENDING
PRAI US 1999-141363P 19990628 (60)
US 1999-168060P 19991130 (60)
US 2000-177836P 20000125 (60)
US 2000-178368P 20000127 (60)
DT Utility
FS APPLICATION
LREP PATREA L. PABST, HOLLAND & KNIGHT LLP, SUITE 2000, ONE ATLANTIC CENTER, 1201 WEST PEACHTREE STREET, N.E., ATLANTA, GA, 30309-3400
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN 12 Drawing Page(s)
LN.CNT 2441
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the production of purified, catalytically active, **recombinant memapsin 2** have been developed. The substrate and subsite specificity of the catalytically active enzyme have been determined. The substrate and subsite specificity information was used to design substrate analogs of the natural **memapsin 2** substrate that can **inhibit** the function of **memapsin 2**. The substrate analogs are based on peptide sequences, shown to be related to the natural peptide substrates for **memapsin 2**. The substrate analogs contain at least one analog of an amide bond which is not capable of being cleaved by **memapsin 2**. Processes for the synthesis of two substrate analogs including isosteres at the sites of the critical amino acid residues were developed and the substrate analogs, OMR99-1 and OM99-2, were synthesized. OM99-2 is based on an octapeptide Glu-Val-Asn-Leu-Ala-Ala-Glu-Phe (SEQ ID NO:28) with the Leu-Ala peptide bond substituted by a transition-state **isostere** hydroxyethylene group (FIG. 1). The **inhibition** constant of OM99-2 is 1.6.times.10.sup.-9 M against **recombinant** pro-**memapsin 2**. Crystallography of **memapsin 2** bound to this **inhibitor** was used to determine the three dimensional structure of the protein, as well as the importance of the various residues in binding. This information can be used by those skilled in the art to design new **inhibitors**, using commercially available **software programs** and techniques familiar to those in organic chemistry and enzymology, to design new **inhibitors** to **memapsin 2**, useful in **diagnostics** and for the **treatment** and/or **prevention** of **Alzheimer**'s disease.

L6 ANSWER 17 OF 22 USPATFULL on STN
AN 2000:7289 USPATFULL
TI Human nucleic acid binding protein
IN Bandman, Olga, Mountain View, CA, United States
Au-Young, Janice, Berkeley, CA, United States
Hawkins, Phillip R., Mountain View, CA, United States
Hillman, Jennifer L., San Jose, CA, United States
PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 6015788 20000118
AI US 1998-195855 19981119 (9)
RLI Division of Ser. No. US 1996-698407, filed on 15 Aug 1996, now patented, Pat. No. US 5856128
DT Utility
FS Granted

EXNAM Primary Examiner: Sisson, Bradley; Assistant Examiner: Longton, Enrique D.
LREP Sather, Susan K.Incyte Pharmaceuticals, Inc.
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 11 Drawing Page(s)
LN.CNT 1830
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides polynucleotides which identify and encode a novel human nucleic acid binding protein (NABP). The invention provides for genetically engineered expression vectors and host cells comprising the nucleic acid sequences encoding NABP. The invention also provides for the use of substantially purified NABP or its antagonists, in pharmaceutical compositions for the **treatment** of diseases associated with the expression of NABP. Additionally, the invention provides for the use of antisense molecules to NABP in pharmaceutical compositions for **treatment** of diseases associated with the expression of NABP. The invention also describes **diagnostic** assays which utilize **diagnostic** compositions comprising the polynucleotide, fragments or the complement thereof, which hybridize with the genomic sequence or the transcript of polynucleotides encoding NABP or anti-NABP antibodies which specifically bind to NABP.

L6 ANSWER 18 OF 22 USPATFULL on STN
AN 1999:1467 USPATFULL
TI Human nucleic acid binding protein
IN Bandman, Olga, Mountain View, CA, United States
Au-Young, Janice, Berkeley, CA, United States
Hawkins, Phillip R., Mountain View, CA, United States
Hillman, Jennifer L., San Jose, CA, United States
PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5856128 19990105
AI US 1996-698407 19960815 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Wax, Robert A.; Assistant Examiner: Longton, Enrique D.
LREP Billings, Lucy J.Incyte Pharmaceuticals, Inc.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1776
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides polynucleotides which identify and encode a novel human nucleic acid binding protein (NABP). The invention provides for genetically engineered expression vectors and host cells comprising the nucleic acid sequences encoding NABP. The invention also provides for the use of substantially purified NABP or its antagonists, in pharmaceutical compositions for the **treatment** of diseases associated with the expression of NABP. Additionally, the invention provides for the use of antisense molecules to NABP in pharmaceutical compositions for **treatment** of diseases associated with the expression of NABP. The invention also describes **diagnostic** assays which utilize **diagnostic** compositions comprising the polynucleotide, fragments or the complement thereof, which hybridize with the genomic sequence or the transcript of polynucleotides encoding NABP or anti-NABP antibodies which specifically bind to NABP.

L6 ANSWER 19 OF 22 USPATFULL on STN
AN 1998:143904 USPATFULL
TI Directed evolution of novel binding proteins
IN Ladner, Robert Charles, Ijamsville, MD, United States
Gutterman, Sonia Kosow, Belmont, MA, United States
Roberts, Bruce Lindsay, Milford, MA, United States

Markland, William, Milford, MA, United States
Ley, Arthur Charles, Newton, MA, United States
Kent, Rachel Baribault, Boxborough, MA, United States
PA Dyax, Corp., Cambridge, MA, United States (U.S. corporation)
PI US 5837500 19981117
AI US 1995-415922 19950403 (8)
RLI Continuation of Ser. No. US 1993-9319, filed on 26 Jan 1993, now patented, Pat. No. US 5403484 which is a division of Ser. No. US 1991-664989, filed on 1 Mar 1991, now patented, Pat. No. US 5223409 which is a continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990, now abandoned which is a continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Ulm, John
LREP Cooper, Iver P.
CLMN Number of Claims: 43
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 16 Drawing Page(s)
LN.CNT 15973
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin **inhibitor**, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

L6 ANSWER 20 OF 22 USPATFULL on STN
AN 96:101466 USPATFULL
TI Directed evolution of novel binding proteins
IN Ladner, Robert C., Ijamsville, MD, United States
Guterman, Sonia K., Belmont, MA, United States
Roberts, Bruce L., Milford, MA, United States
Markland, William, Milford, MA, United States
Ley, Arthur C., Newton, MA, United States
Kent, Rachel B., Boxborough, MA, United States
PA Protein Engineering Corporation, Cambridge, MA, United States (U.S. corporation)
PI US 5571698 19961105
AI US 1993-57667 19930618 (8)
DCD 20100629
RLI Continuation of Ser. No. US 1991-664989, filed on 1 Mar 1991, now patented, Pat. No. US 5223409 which is a continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990, now abandoned which is a continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Ulm, John
LREP Cooper, Iver P.
CLMN Number of Claims: 83
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 16 Drawing Page(s)

LN.CNT 15323
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin **inhibitor**, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

L6 ANSWER 21 OF 22 USPATFULL on STN
AN 95:29292 USPATFULL
TI Viruses expressing chimeric binding proteins
IN Ladner, Robert C., Ijamsville, MD, United States
Guterman, Sonia K., Belmont, MA, United States
Roberts, Bruce L., Milford, MA, United States
Markland, William, Milford, MA, United States
Ley, Arthur C., Newton, MA, United States
Kent, Rachel B., Boxborough, MA, United States
PA Protein Engineering Corporation, Cambridge, MA, United States (U.S. corporation)
PI US 5403484 19950404
AI US 1993-9319 19930126 (8)
RLI Division of Ser. No. US 1991-664989, filed on 1 Mar 1991, now patented, Pat. No. US 5223409 which is a continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990, now abandoned which is a continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988, now abandoned
PRAI WO 1989-3731 19890901
DT Utility
FS Granted
EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Ulm, John D.
LREP Cooper, Iver P.
CLMN Number of Claims: 49
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 16 Drawing Page(s)
LN.CNT 14368
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin **inhibitor**, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

L6 ANSWER 22 OF 22 USPATFULL on STN
AN 93:52487 USPATFULL
TI Directed evolution of novel binding proteins
IN Ladner, Robert C., Ijamsville, MD, United States
Guterman, Sonia K., Belmont, MA, United States
Roberts, Bruce L., Milford, MA, United States
Markland, William, Milford, MA, United States
Ley, Arthur C., Newton, MA, United States
Kent, Rachel B., Boxborough, MA, United States
PA Protein Engineering Corp., Cambridge, MA, United States (U.S. corporation)
PI US 5223409 19930629
AI US 1991-664989 19910301 (7)
RLI Continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990, now abandoned And a continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Ulm, John D.
LREP Cooper, Iver P.
CLMN Number of Claims: 66
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 16 Drawing Page(s)
LN.CNT 15410
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin **inhibitor**, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

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